"Changing your lifestyle to suit an antipsychotic? Can exercise reduce antipsychotic weight gain for those with Schizophrenia?"

Abstract:

This body of research was conducted through a literature review of studies indicating weight-gain attributable to anti-psychotic medications, and whether exercise can reduce this potential occurrence. Within the review, Quantitative research methods facilitated researchers to analyse the metabolic changes in serum glucagon and lipid production among participants being administered with anti-psychotic medications such as: Olanzapine (Zyprexa), Solian (Quetiapine), Serenace (Haloperidol), Risperidol (Risperidone). Qualitative research methods assisted this researcher, to understand the psychological effect, anti-psychotic weight gain has on an individual(s) experiencing mental health difficulties.

Within mental illness it is has been found that a person is more likely to gain weight within their illness. Be it due to: social isolation, stigma or low self-esteem combined with unhealthy dietary choices. This outcome is increased even further with psychopharmacological interventions. This trend became evident in clinical trials where those treated with: Haloperidol, 18% had weight gain greater than 5 kgs; Risperidone, 24.7% had weight gain > 5kgs; Quetiapine, 0.00; Olanzapine, 40.8% had weight gain > 5kgs. Patient relapse is a phenomenon that is arguably attributable to medication non-compliance. Weight gain is noted within this body of research as a reason why some patients stop taking their medication. Weight gain, non-compliance, equalling relapse is a simplistic analysis of an observable fact that is difficult to quantify, perhaps due, in some degree to the complexities of mental illness. There is unequivocal evidence, exercise is of potential benefit to everyone, however such advice is at times difficult to heed. Perhaps, even more so, when a person’s decision making
skills are influenced by mental health difficulties. Such difficulty is examined in this body of research, through qualitative research using: focus group, randomised control trials, naturalistic and grounded theory methods; all contributing to provide valued information from a patient’s perspective. This research will further help to provide those working with individuals experiencing mental health difficulties, an opportunity to empathise with those in our care as they battle the challenges, of diagnosis and treatment, within their illness.

**Keywords:** Antipsychotic weightgain; Qualitative research, Quantitative research, Mixed Method Research; Focus Group Research; Grounded Theory; Naturalistic Research; Well-being and Schizophrenia and Anti-psychotic drugs; Exercise to reduce weight-gain; mental illness weight-gain and exercise.

**Introduction.**

A literature review summarises and synthesizes a body of research to; enhance the understanding of a specific area that is important to students and practitioners within a particular profession (Cronin, Ryan and Coughlan, 2008). This assignment is a review of research conducted by health professionals related to the specific area of antipsychotic medications, and their potential to cause weight-gain. All of the quantitative research articles used for this review, indicate weight-gain as a side effect of most antipsychotic medications (Bobe’s et al (2003), Poulin et al (2007), Correll Kane and Manu (2010), Vreeland et al (2003), Hanwella et al (2010) Vidarsdottor et al (2010)). Weight-gain is also a noted side effect in the British National Formula Publication (BNF, 2008) used by professionals in medication management. By including research that uses semi structured and focus group interviews (Fogarty and Happell (2005), McDevitt et al (2008)), randomised control trial (Evans, Newton, and Higgins (2005)) and
grounded theory (Crone and Guy (2008), these qualitative research methods will help us to have a greater understanding of the patient’s experience of any interventions. Through the review of these research studies, they will assist to answer the research question "Changing your lifestyle to suit an antipsychotic? Can exercise reduce antipsychotic weight gain for those with Schizophrenia?"

**Method**

Articles for this review were obtained using keyword searches, only research in English and between 2002 and 2010 were selected from the following databases: Pubmed, Cinahl Plus with Full Text, PsychInfo, Medline and Cochrane Library; which resulted in eighty-three articles being found. The keyword searches used in these databases were: antipsychotics and weight-gain, quantitative research; well-being and Schizophrenia and Antipsychotic drugs, qualitative research; exercise to reduce weight-gain; mental illness weight-gain and exercise. However, although the keyword search resulted in a large number of articles found, only those that helped to answer the research question being of this review, were used. For this purpose only eleven articles were selected. Of this number five were of qualitative design (from Australia (2), United Kingdom (2), United States of America), and six were quantitative (from Spain, Sri Lanka, United States of America (2), Canada and the Netherlands). The number of articles both Qualitative and Quantitative would lend this review to being potentially, a Mixed Method Review. By combining both methods of research, as Creswell and Tashakkori (2007) discuss, “can serve the dual purpose of consideration and elaboration of results” (page 109). The objective is to provide helpful information for nursing in Psychiatric settings, in order to assist with; maintaining patient medication compliance and most importantly to promote positive mental health.
The Qualitative studies for this review used some of the following methods; naturalistic, grounded theory (Crone and Guy, 2008), randomised control trial (Evans, Newton and Higgins (2005), and focus group interviews (Fogaty and Happell (2005), McDevitt et al (2006)), with Faulkner and Biddle (2002) using telephone and face to face interviews; all using comprehensive data analysis. Some of the following methods were used for the quantitative studies: The Framingham method/score with random selection (Correll, Kane and Manu (2010)), Data Analysis of a weight program intervention (retrospective analysis Vreeland et al (2003)), analysis of covariance, and control group trials. Research in the literature reviews was undertaken in: university research facilities, also hospital and community settings within mental health services.

**Findings**

The literature reviewed comprehensively discusses that antipsychotics do induce weight gain and that psychoeducation interventions can be helpful to minimise or control this antipsychotic side effect. The importance of weight gain as a side-effect of medication; is that it can result in patient non-compliance, which unfortunately can lead to relapse, resulting in some cases of repeated hospitalisation (Barker, 2003). This causes increased cost to the health service, and most importantly delays patient recovery and their potential to participate positively and fully in society (Barker). These areas are why this literature review of the research is of added importance within Psychiatric nursing today, as services become more recovery orientated and community based (Barker). This review will begin by looking at the data obtained which verifies biochemical variance among people receiving certain anti-psychotic medications. Hence it will be shown that weight-gain is a side-effect within the majority of psychotropic medications.
Bobes et al (2003) used a descriptive quantitative study with clinical trials to maximise reliability and validity of the research (Fink, 2010). Combined with a Scandanavian side-effects rating scale (UKU); in which they study; Weight gain in patients with schizophrenia treated with Risperidone, Olanzapine, Quetiapine or haloperidol. The large sample of participants used, 636 eventually evaluated out of 691, does not make the research generalisable however gives evidence of weight-gain relative to specific antipsychotics used within their trial. The diagnosis of Schizophrenia in this and the other trials reviewed was determined according to the criteria for diagnosis within the DSM IV (APA, 2000).

Bobe’s et al obtained their data retrospectively, from patient charts, and was analysed using the SPSS (version 10) statistical package.

Although Obesity and the development of Type 2 Diabetes in particular, is of concern to all developed countries (Allison et al (1999), Poulin et al (2007), Bobe’s et al, Hanwella et al (2010), Vancampfort et al (2009)), Bobes et al’s (2003) findings show a greater prevalence of weight-gain in patients being treated with antipsychotics. The results concluded that on average between, the four antipsychotics measured: Haloperidol (trade name used in Ireland, Serenace), Olanzapine (Zyprexia), Quetiapine (Seroquel) and Risperadone (Risperadol), only Quetiapine showed no noticeable weight-gain. However, a limitation of this research was the fact that Quetiapine is a relatively new antipsychotic, and therefore is not as widely prescribed as the other medications, such as Haloperidol, which was mostly being prescribed to those older participants in the study who have been treated over a longer period. There was significance of weight-gain between the medications within this research (table 1. Appendix), as proportionately more people were treated with Olanzapine (133) but the number of participants evaluated in total was quite
low and the sample sizes in each group of medications was variable not allowing for statistical significance.

The researchers note the use of Quetiapine as a limitation and go on to explain the exclusion and inclusion criteria as being a contributing factor in this. It excluded those patients who no longer received the specified medication and only included those who tolerated the specific medication. For example, a number of patients were discontinued on medication as it became intolerable, or the side effect of weight gain. The results concluded that those patients using Olanzapine (Zyprexa) are most susceptible to weight gain than users of Haloperidol and Respiradone. However bias could be introduced as the Bobes et al (2003) study was funded by the Pfizer pharmaceutical company and Olanzapine is manufactured by a competitor, and as the study reveals, weight gain is more prevalent in those being treated with Olanzapine. Similarly Dr. Correll, Dr. Kane and Dr. Manu (Correll, Kane and Manu, 2010) have affiliations with a number of pharmaceutical companies, a conflict of interest that is duly noted in their research. Although, undoubtedly the affiliation is of scientific significance to the pharmaceutical industry; it is arguably just as important to Psychiatry?

Another limitation discussed in the Bobe’s et al research, was the data collection method for weight gain was using a “modified” version of the UKU scale (Lingjaerde et al (1987), Ivarson et al (2010)) which according to the authors, was not specifically designed for evaluation of the side effect “weight gain”. There was no mention of the specific modifications to the scale used or whether the modified scale was then tested and retested to improve reliability and validity (Montejo et al, 2011). However the data analysis was adequately described and appropriate with tables that explained the measurements obtained and affective for their research question, similarly as in the
research conducted by Poulin et al (2007), Correll Kane and Mann (2010), Vreeland et al (2010), Hanwella et al (2010). The research made good use of tables and charts, for example in Table 1 (see appendices) it is evident that those study participants treated with Olanzapine had greater evidence of a weight-gain percentage.

Vidarsdottir et al (2010) compliments the data collected in Bobe’s et al study. The Quantitative research method used, has in-depth analysis of glucose and lipid metabolism in patients treated with two different antipsychotic medications. This factor is also evident in research conducted by others used in this review (Vreeland et al (2003), Hanwella et al (2010), Correll, Kane and Manu (2010)). Vidarsdottir and colleagues received ethical consent from the Leiden University Medical Centre and written consent from the participants. Ethical and participatory consent was present in all the studies. For their research Vidarsdottir et al, recruited fourteen healthy men aged between 20 and 40 years. Volunteers were recruited through a newspaper advertisement, this method of recruitment eliminates potential bias, and has the added affect of reaching and informing a larger population of the study’s aims (Sifaneck and Neaigus, 2001). The exclusion criteria were: those receiving antipsychotic treatment, smokers, or on medications that affected the central nervous system. This enabled the researchers to validate the effects of antipsychotic medication (Olanzapine and Haloperidol) on the metabolism of healthy males. However a number of subjects were replaced in this particular trial as they had incidence of medication side-effects, particularly with haloperidol. Side-effects including: acute dystonia and restlessness. Those excluded were then replaced by new volunteers. These side effects are also noted by the other researchers in this review.
The data was collected over an eight day period, and analysed using a windows program SPSS (Version 12.0), which is used for statistical analysis in social sciences (a newer version of the data analysis package used by Bobe’s et al (2003) in their study).

Vidarsdottir et al’s (2010) research indicates a marked increase in serum glucagon concentrations over the seven day period, for the group being treated with Olanzapine (Table 2. Appendix). However serum glucagon levels were of no statistical significance for those being administered the typical antipsychotic Haloperidol. An increase in the serum glucagon levels affects lipid metabolism resulting in potential weight-gain, and Obesity; which can progress to diabetes and cardio vascular difficulties (Solerte et al, 1999). Although atypical antipsychotics reportedly have fewer extra pyramidal side-effects than typical antipsychotics (Healy, 2009), a noted increase in weight-gain in the early phase of treatment, supports the theory of weight-gain, even in healthy individuals treated with Olanzapine. However the sample size (N=14) is very low and therefore prevents generalisability.

Another anti-psychotic with notable weight-gain as a side effect is Clozaril. Initially introduced in the 1950’s, it was taken off the market due to fatalities among patients being administered with it. Interestingly Clozaril is widely used today (Healy, 2009).

Hanwella et al (2010), in a study of patient’s being treated with Clozapine, note a large proportion of the literature available suggests weight gain over a ten week period, averaging 4.45 kilograms. There were only three participants in this study therefore it is not generalisable; also it notes a limitation being that two authors received educational grants from pharmaceutical companies, which could introduce bias.
The Hanwella et al study is of particular interest to this reviewer as within the findings was the incidence of a participant, who prior to commencement on Clozapine (Clozaril), was receiving an oral anti-diabetic medication. However after three years of treatment with the anti-psychotic, has normalised her blood sugar levels without the need for medication. So although antipsychotics, according to the literature in this review, are known to induce weight gain as a side effect, this particular participant’s actual weight-loss since commencement on Clozaril has normalised her blood sugars? Diabetes mellitus is symptom of obesity in society today as already outlined and unfortunately weight gain among those with mental illness is prominent due in some cases to medication side effects (Bobe’s et al (2003), Poulin et al (2007), Correll Kane and Manu (2010), Vreeland et al (2010), Hanwella et al (2010) Vidarsdottor et al (2010)) and lifestyle.

While being treated with the antipsychotic Clozaril, a patient develops any signs of Agranulocytosis or Neutropenia, they are immediately discontinued from this treatment (BNF, 2008). This has resulted in medication being changed, in some cases to Olanzapine (Healy, 2009), which as the literature here suggests, is associated with the side effect of weight-gain.


Using a randomized controlled trial, Evans, Newton and Higgins (2005); recruited participants through a local mental health service in Australia. The trial involved fifty-one people who were either assigned to an intervention group (N=29), whom received education sessions on health and
well-being, while the control group (N=22) received no intervention at all. Qualitative research combined with random control trials are the most highly recommended standard of qualitative research; as they provide valid and reliable data of patient experiences (Rogers et al 2003).

There has been research into the nursing supports that can help to minimise the side-effect of weight-gain (Mensa et al (2004), Littrell et al (2003)); the verifiable positive improvements are supportive of psycho-educational interventions (Vreeland et al, 2003). As well as using randomised controlled trials in Qualitative research for reliability and validity, the use of Service users themselves to conduct research is also highly commended though, very rare. Crone and Guy (2008) combine research knowledge with the personal experience of mental illness for one of their researchers, when conducting focus group interviews with people in a health service facility in Southeast England. They used a purposive sample as it facilitates the collection of specific data that will develop further constructive discussion within the setting about service user health promotion (Fink 2010). The welcome addition of service user perspective in the reviews provides valuable insight into the positive impact exercise could have and, is the essence of grounded theory where the data collected guides the researchers toward new understandings of service user perspectives (Broussard, 2006). All of the studies included service user direct quotes and provided rigorous data analysis of transcribed verbatim from interviews undertaken. However Gone and Guy (2008) in their research do acknowledge that it was taken for granted that participants were aware of the benefits of exercise, as it turns out that the study group just went along with the intervention as it had become part of their daily routine without thinking about the studies implications?
Although the quantitative studies provide validated data that lends itself to the conclusion of weight-gain from anti-psychotic medications as Vidarsdottir et al (2010) and others reviewed here discuss. The qualitative articles reviewed have shown that, through service user participation and interviews, exercise can improve mental well-being; and this is corroborated by researchers in this field (Green et al 2000, Faulkner and Biddle 2002, Pelham et al 1993). However, the presence of weight-gain as a side-effect is an additional concern for patients dealing with mental illness, and in some cases patients would rather not take this medication as a result (Correll, Kane and Manu, 2010).

**Conclusion**

In conclusion, the quantitative research conclusively detail, the effects of anti-psychotic medications on metabolism resulting in weight-gain, depending of course on the medication. Alternately the qualitative research looked at the patient’s experience and how psycho-educational interventions can improve your mental and physical health. From a nursing perspective it has been valuable to see the comprehensive data collections that verify anti-psychotic weight-gain, and to gain a greater understanding of why this occurs. Similarly the qualitative research has been a stark reminder to engage with patients on a number of levels: educational, therapeutically and with empathy. If at such a difficult time for patients, psychiatric nurses can provide interventions that can empower them to make positive choices about their health, then “Changing your lifestyle to suit your health. Through psycho-education you can change the weight-gain effects of antipsychotics”, may now be the revised research question used in this review. For it has been shown and discussed about the metabolic changes that can occur due to anti-psychotic medications, but the evidence from the research reviewed here
shows that exercise can minimise weight-gain. As this client in Crone and Guy (2008) mentions after sports therapy:

“I find that if I do exercise in the day I have achieved something and therefore it makes me feel happier in myself, and at the end of the day, I know it is only exercise and it is not working or anything, but to me it is something that keeps me going.” (Pg. 204)
Appendix

Table 1: Percentage weight gain per medication administered (Bobe’s et al 2003).

<table>
<thead>
<tr>
<th>Psychotropic Medication</th>
<th>Weight-gain (&gt;5 kg percentage of participants)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Haloperidol</td>
<td>18.2</td>
</tr>
<tr>
<td>Olanzapine</td>
<td>40.8</td>
</tr>
<tr>
<td>Rispiradone</td>
<td>24.7</td>
</tr>
<tr>
<td>Quetiapine</td>
<td>0.00</td>
</tr>
</tbody>
</table>

TABLE 2. Metabolic variables during hyperinsulinemic euglycemic clamp (Vidarsdottir et al 2010)

<table>
<thead>
<tr>
<th></th>
<th>Olanzapine (n = 7)</th>
<th>Haloperidol (n = 7)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Day 0</td>
<td>Day 8</td>
</tr>
<tr>
<td>Glucose (mmol/liter)</td>
<td>4.6 ± 0.2</td>
<td>4.5 ± 0.4</td>
</tr>
<tr>
<td>Insulin (mU/liter)</td>
<td>71.6 ± 2.3</td>
<td>72.6 ± 2.8</td>
</tr>
<tr>
<td>Background enrichment of [6,6-2H2] glucose (% of total glucose)</td>
<td>1.33 x 10^{-2} ± 0.07 x 10^{-2}</td>
<td>1.29 x 10^{-2} ± 0.04 x 10^{-2}</td>
</tr>
<tr>
<td>GIR (mg · kg^{-1} · min^{-1})</td>
<td>6.3 ± 0.9</td>
<td>4.9 ± 0.9¹</td>
</tr>
<tr>
<td>Glucose disposal (mg · kg^{-1} · min^{-1})</td>
<td>8.2 ± 0.9</td>
<td>6.9 ± 0.8¹</td>
</tr>
<tr>
<td>EGP basal (mg · kg^{-1} · min^{-1})</td>
<td>2.6 ± 0.10</td>
<td>2.6 ± 0.12</td>
</tr>
<tr>
<td>EGP hyperinsulinemic (mg · kg^{-1} · min^{-1})</td>
<td>1.9 ± 0.06</td>
<td>2.0 ± 0.15</td>
</tr>
<tr>
<td>EGP % inhibition</td>
<td>25.9 ± 1.8</td>
<td>21.0 ± 4.7</td>
</tr>
<tr>
<td>Ra glycerol basal (µmol · kg^{-1} · min^{-1})</td>
<td>2.5 ± 0.27</td>
<td>2.5 ± 0.30</td>
</tr>
<tr>
<td>Ra glycerol hyperinsulinemic (µmol · kg^{-1} · min^{-1})</td>
<td>2.1 ± 0.10</td>
<td>2.1 ± 0.14</td>
</tr>
<tr>
<td>Ra glycerol % decline</td>
<td>16.4 ± 5.9</td>
<td>15.4 ± 7.1</td>
</tr>
<tr>
<td>FFA % decline</td>
<td>83.2 ± 2.2</td>
<td>65.3 ± 6.9¹</td>
</tr>
<tr>
<td>TG % decline</td>
<td>17.0 ± 3.6</td>
<td>8.1 ± 3.6²</td>
</tr>
</tbody>
</table>

Values are expressed as mean ± SEM. EGP % inhibition, Decline of EGP during hyperinsulinemia expressed as percentage of basal value; FFA % decline, decline of circulating FFA during hyperinsulinemia expressed as percentage of basal value; Ra, rate of appearance; TG % decline, decline of circulating TG during hyperinsulinemia expressed as percentage of basal value.¹ P < 0.05 vs. d 0. ² P < 0.01 vs. d 0.
Bibliography:

Searching: CINAHL Plus with Full Text; Search terms; MW Exercise and Mental health; PsychInfo: Search terms; TX Antipsychotic drugs and TX Weight gain and TX Exercise Limiters - Full Text; Published Date from: 20020101-20101231; Exclude Book Reviews; Age Groups: Adulthood (18 yrs & older); Methodology: -Quantitative Study Expanders - Apply related words; Search modes - Boolean/Phrase

PsychInfo (EBSCOhost): Search terms; well being and Schizophrenia and Antipsychotic drugs. Search options; Limiters - Linked Full Text; References Available; Published Date from: 20020101-20101231; Peer Reviewed ;Search modes - Boolean/Phrase

MEDLINE(EBSCOhost) Search terms; TX Mental illnes and TX Weight gain and TX Exercise; Limiters - Linked Full Text; Abstract Available, Search modes - Boolean/Phrase

Additional resources


Naber, D, & Lambert, M 2009, 'The CATIE and CUtLASS studies in schizophrenia: Results and implications for clinicians', CNS Drugs, 23, 8, pp. 649-659, PsycoINFO, EBSCOhost, viewed 24 February 2011.

Nash, M 2010, 'Assessing nurses' propositional knowledge of physical health', Mental Health Practice, 14, 2, pp. 20-23. EBSCOhost, viewed 24 February 2011.


Truman, C, & Raine, P 2002, 'Experience and meaning of user involvement: some exploration from a community mental health project', Health & Social Care in the Community, 10, 3, pp. 136-143, EBSCOhost, viewed 24 February 2011.
Reference list:


Crone, D, & Guy, H 2008, 'I know it is only exercise, but to me it is something that keeps me going': a qualitative approach to understanding mental health service users' experiences of sports therapy'. *International Journal of Mental Health Nursing*, 17, 3, pp. 197-207. EBSCOhost, viewed 24 February 2011.


Vidarsdottir, S., de Leeuw van Weenen, J E., Frolich, M., Roelfsema, F., Romijn, J A., Pijl,H.